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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/934,970	08/21/2001	Jose L. Boyer	03678.0064.CPUS01	8356

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EXAMINER
LEWIS, PATRICK T

ART UNIT	PAPER NUMBER
1623	

DATE MAILED: 10/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/934,970

Applicant(s)

BOYER ET AL.

Examiner

Patrick T. Lewis

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 30 July 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 2-25 is/are pending in the application.
- 4a) Of the above claim(s) 2 and 16-21 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 3-15 and 22-25 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>07302004</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group II in Paper No. 6 dated July 3, 2003 is acknowledged.
2. Claims 2 and 16-21 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on July 3, 2003.

Applicant's Response Dated July 30, 2004

3. In the Response filed July 30, 2004, the specification was amended, and claims 12 and 22-23 were amended.
4. Claims 2-25 are pending. Claims 2 and 16-21 are drawn to a nonelected invention. An action on the merits of claims 3-15 and 22-25 is contained herein below.
5. The rejection of claims 22-23 under 35 U.S.C. 112, second paragraph, has been rendered moot in view of applicant's amendment filed July 30, 2004.
6. Applicant's arguments with respect to claims 3-15 and 22-25 under 35 U.S.C. 103(a) have been considered but are moot in view of the new ground(s) of rejection.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

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(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

8. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

10. Claims 3-15 and 22-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of Zamecnik US 5,049,550 (Zamecnik); Beigelman et al. US 6,528,640 (Biegelman); and Markland et al. US 5,814,609 (Markland).

Claims 3-15 and 22-25 are drawn to a method of preventing or treating diseases or conditions associated with platelet aggregation comprising administering to a subject a pharmaceutical composition comprising a therapeutic effective amount of a P2Y₁₂

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receptor antagonist compound, wherein said amount is effective to bind P2Y₁₂ receptors on platelets and inhibit ADR-induced platelet aggregation. The P2Y₁₂ receptor antagonist is limited to a dinucleotide compound of Formula I. Dependent claims limit the conditions or diseases treated or prevented and modes of administration. Claims 8-12 limit the method by requiring the administration of a fibrinolytic agent.

Zamecnik teaches the use of diadenosine 5',5'''-p¹,p⁴-tetraphosphate (AP₄A), or an analogue thereof, as an antithrombotic agent (column 3, lines 4-59). The invention is based on the discovery that the administration of exogenous AP₄A, or an analogue thereof, to a mammal inhibits platelet aggregation, and, therefore, reduces the incidence of thrombosis. Zamecnik further suggest using AP₄A as a model to design similar or more efficacious agents (e.g., synthetic analogs).

Zamecnik differs from the instantly claimed invention in that Zamecnik does not explicitly teach analogs wherein at least one of the 2'- or 3'-positions is OR₁ or OR₂ as instantly claimed. Although Zamecnik does not explicitly teach the dinucleotides as P2Y₁₂ receptor antagonists, Zamecnik teaches the use of AP₄A and corresponding analogs for the inhibition of platelet aggregation. Zamecnik does not teach the use of AP₄A or analog thereof in combination with a fibrinolytic agent.

Biegelman teaches that oligonucleotides are modified to enhance stability and/or enhance biological activity by modification with nuclease resistant groups, for example, 2'-amino, 2'-C-allyl, 2'-fluoro, 2'-O-methyl, 2'-H, nucleotide base modifications 9column 16, lines 51-58; column 17, line 41 to column 18, line 6). Therapeutic nucleic acid molecules delivered exogenously must optimally be stable within cells until translation of

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the target RNA has been inhibited long enough to reduce the levels of the undesirable protein.

Markland teaches compositions for the prevention of thrombus formation comprising contortrostatin (CN) and at least one thrombolytic agent (column 12, lines 6-32). Suitable thrombolytic agents include anisoylated plasminogen streptokinase activator complex (APSAC); tissue-type plasminogen activator (tPA); urokinase-type plasminogen activator (uPA); and fibrolase, a snake venom fibrinolytic agent.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the 2'-position of the AP₄A in order to find more efficacious antithrombotic agents. One of ordinary skill would have been motivated to modify the 2'-position based on the teachings of Beigelman which teaches enhanced stability and/or enhance biological activity by modification of the 2'-position with nuclease resistant groups such as 2'-O-methyl. It would have also been obvious to a person of ordinary skill in the art at the time the invention was made to use the compounds of the instant invention in combination with a fibrinolytic agent to treat various diseases associated with platelet aggregation. The use of materials in combination, each of which is known to function for an intended purpose (i.e., inhibition of platelet aggregation), is *prima facie* obvious.

Conclusion

11. Claims 2-25 are pending. Claims 2 and 16-21 are drawn to a nonelected invention. Claims 3-15 and 22-25 are rejected. No claims are allowed.

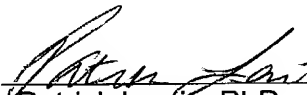
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Contacts

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patrick T. Lewis whose telephone number is 571-272-0655. The examiner can normally be reached on Monday - Friday between 10 am - 2 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


Patrick Lewis, PhD
Examiner
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